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THE UNIVERSITY OF TORONTO MEDICAL JOURNAL

(An Undergraduate Publication)

This journal is published seven times a year, November to May, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

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Volume X TORONTO, JANUARY, 1933 Number 3

EDITORIAL

MEDICAL EDUCATION.

The Final Report of the Commission on Medical Education of the Association of the American Medical Colleges has just come to our hands. This report is the result of seven years' work by the Commission, investigating all phases of medical education in North America and also in some respects in Europe. The Commission has made a most exhaustive survey of the matter and present a most interesting and comprehensive report of their findings.

There are many matters discussed in the report which should be of extreme interest to the undergraduate in medicine.

The Commission was established in 1925 to study the educational principles involved in medical education and licensure and to make suggestions which would be an aid in adapting the medical education to the needs of the community. Thus we have a concrete picture of just how well the medical profession is equipped to bring to the service of humanity the multitude of knowledge which has been accumulated in the science of medicine. One of the factors, and probably the most important factor which has necessitated such far-reaching changes in the profession in the recent past is the fact that during the past sixty years more medical knowledge has been accumulated than during the previous four thousand. That changes in methods of teaching are necessary is obvious. The placing of this knowledge at the service of the

public is indeed a most difficult problem.

The question of the economic problem facing the public is touched upon to some extent. It is emphasized that some relief must be given to the vast majority of the public in the matter of being able to obtain adequate medical attention. However, particular mention is made of the fact that, no matter what form of medical service is ultimately organized for this purpose, all attempts should be made to preserve the individual patient as the unit of medical practice. It is stressed that we cannot apply "mass production" in medicine to such a complex and variable physical and mental makeup as that possessed by a human being.

The report refers to the increasing numbers of medical practitioners and points out that there is no longer any need for as high a ratio of physicians to population as before because of the fact that with the development of so many aids to practice, a physician is enabled to care for a greater number of people. The distribution of physicians is tending toward the urban centres; the Commission believes, however, that this problem can best be overcome by means of the more rapid methods of transportation and the establishment of more clinics, hospital centres and nursing facilities.

Specialists have a definite part in the provision of medical services to the community. It is urged that specialists be registered as such so that the public will be made aware of this fact, and also to assure that all specialists have had adequate training. The place of post-graduate "refresher" courses and internships have become of increasing importance in medicine and should be fostered to as great an extent as possible.

In dealing with the problem of the medical school it is pointed out that there has been a considerable change in the more recent years in the method of attack upon medical teaching. It has been accepted as impossible to impart to the medical student all the knowledge available; therefore it is attempted to equip the graduate with a knowledge of the basic principles of anatomy, physiology, biochemistry, pathology and bacteriology, physical examination, history taking, and diagnosis. It is considered better to give the student a means by which he can discriminate the useful and useless information, and to appreciate the meanings of organic and functional change. than to load him with a great deal of detail which for the most part will be forgotten and may not prove very useful. There is a tendency to make the student a unit of education as important as the lectures, clinics, and the faculty, that is, the idea that all true education is self-education is rapidly being made part of the medical education program.

The University of Toronto was represented on the Commission by Sir Robert Falconer. There are many references to our Medical Faculty, indicating that it is with the leaders on the American continent. It is interesting to note that our undergraduate registration is the highest of any medical faculty in North America.

INTERNSHIP.

Dr. Harvey Agnew has very kindly consented to write for us an article upon the duties of an intern, which article appears in this issue. While this article is of most interest at the present time to the graduating year, nevertheless we believe that it would be most valuable for the members of the lower years to read it, so that they will be able to look forward to their internship in the right light.

Dr. Agnew, as Secretary of the Department of Hospital Service of the Canadian Medical Association, can give us an insight into this problem which very few can give. We welcome the opportunity of being able to publish this article

YOUR INTERNSHIP---MAKING IT WORTH WHILE

By HARVEY AGNEW, M.D.,
Secretary, Department of Hospital Service, Canadian Medical Association.

Few decisions so profoundly affect the future of the medical student as his decision with respect to internship. His choice, judging from the experience of so many others, may determine the bent of his professional interest, perhaps his specialty, frequently the location of his practice, and, not infrequently, his domestic status. While it is quite impossible to foresee what fate holds in store, nevertheless it is most important that this vital transition period, this introduction to the diverse perplexities and responsibilities of clinical practice, be under the best possible associations. There is no question any more about the value of internship; in fact, it is fast becoming obligatory as an essential stage of the student's training, and it is generally recognized that a good general rotating internship is a sound professional background no matter what speciality may be taken up later.

The Purposes Of Internship.

An internship implies a two-sided bargain; therefore two viewpoints must be borne in mind: (a) that of the intern, and (b) that of the hospital. Unless each participant respects the needs of the other, dissatisfaction is bound to result.

(a) *The Viewpoint of the Intern.*—The intern has one prime objective, namely, to supplement his more academic undergraduate training with that practical experience which he realizes to be an essential qualification for practice. Fundamentally, his is still the educational viewpoint; he wants to see all that is visible, palpate everything palpable, and have an opportunity of participating in all those clinical procedures with which he anticipates being faced in the future.

(b) *The Viewpoint of the Hospital.*—The hospital exists primarily to heal the sick; therefore the chief value of the intern to the hospital lies in his service to the patient—by doing dressings, writing histories, carrying out clinical procedures, such as intravenous medications or catheterizations, assisting in the operating room, giving first aid in the emergency room, and, in general, functioning as the representative of the medical staff. Unless the intern is available for the various duties, and unless he does them faithfully and efficiently, he is of little or no value to the hospital. Actually he may be a distinct liability, for it costs money to provide him with maintenance and laundry. Interns are notoriously hard on rubber gloves and syringes, and the hospital may be faced with serious forensic liability for his thoughtlessness or negligence.

Constant appreciation of these two viewpoints would prevent many misunderstandings.

In an effort to acquaint senior students with those hospitals in Canada which make every effort to provide educational opportunities for the intern, the Canadian Medical Association, through its Department of Hospital Service, issues annually a list of hospitals which are approved for internship. In the United States the Council on Medical Education and Hospitals of the American Medical Association has been meeting a similar need for some years. Hospital staffs are co-operating most admirably in improving their services.

Getting The Most From An Internship.

One of the intern's greatest handicaps is his own lack of clinical perspective—because of lack of experience. The relative importance of various phases of his hospital work is difficult to evaluate. How can he know what

will be most helpful to him in practice? He cannot foresee the repeated value to him in the future of some apparently trivial diagnostic point casually mentioned by his chief; he does not know that it is infinitely more important for him to learn to diagnose and meet post-operative complications than to learn the exact technique of a pylorectomy or a lobectomy; it is difficult for him to realize that the experience with early signs and symptoms in the out-patient department will be much more useful in his office practice than most of his knowledge of highly complicated and specialized technique gained upstairs. There are many good and irrefutable reasons why the internship should be taken before entering practice, but its glorious opportunities would be more appreciated could the intern have had more previous contact with the problems of outside practice. One of the best interns at one of our large hospitals a few years ago was a man in his fiftieth year. Submerging his personal pride, he started in de nova, as an utter novice, learning the technique of the more recent clinical procedures, and, above all, finding an answer to the many diagnostic and therapeutic handicaps under which he had laboured for years.

This lack of clinical experience makes it all the more important for the intern to make a thorough and conscientious *self-analysis*—to study his needs, his inclinations, his weaknesses, and so endeavour to remedy the gaps in his medical and psychological preparation that he will be best fitted to compete in the tense struggle of professional life. Likewise, he should make a careful *job-analysis*, to clarify in his own mind his various duties and responsibilities, and to gain a clear concept of his relationship to the hospital. An active sympathetic intern committee can do much to help the intern staff in this respect—if there isn't an intern committee, or if it has gone into hibernation, respectfully ask the medical staff to correct the situation.

With no examinations to face, and with no prescribed curriculum to study, it is exceedingly easy for the intern to let his routine duties constitute his professional day, and early in his year jettison his good resolves to continue his reading. This is a sad mistake, for *combined* observation and reading makes the most effective form of study. Each case should constitute a text for a review of that subject; from the records and with the approval of one's seniors, studies might be made as to the effect of certain drugs or of surgical methods; every effort should be made to perfect oneself in the technique of clinical procedures, such as blood grouping, the handling of wet plaster, blood sugar estimations, the reading of X-ray plates, paracentesis of the ear drum, spinal puncture, etc. If one approaches history writing with an intelligent viewpoint it becomes, not a routine drudgery, but a priceless opportunity to gain a most valuable knowledge of the background of disease. No autopsy, no matter how lacking in promise, should be missed if duties permit attendance. Osler extolled the humbling influence of the postmortem room on the self-assured clinician, and urged the young graduates to haunt the morgue. Take pride in your percentage of autopsy consents.* In nearly all hospitals interns are welcomed to the staff conferences and monthly meetings; take in as many of these as you can, learn the problems of staff-organization and welcome opportunities to prepare case reports for discussion.

The Value Of Time.

At medical school we talk of having to "put in" so many years; we refer to "putting in" one, two or more years at internship. This is the wrong mental attitude. Much better would it be for

* The intern or attending doctor will gain much useful information from an excellent paper, "Means of Securing Postmortem Examinations," by Ralph G. Mills, M.D., which was printed in the Bulletin of the American College of Surgeons, Vol. XIC., No. 4, Dec. 1930, pp. 40-57.

the intern to form the habit of asking himself each night: "How much more do I know to-night than I did this morning?" The intern must get the viewpoint that a definite appraisement should be put upon his time. What is the monetary value of an average year in practice to him?—not his first year in practice, for he will have to go through that period anyway. A conservative estimate in normal times might be five thousand dollars—nearly fourteen dollars a day. In other words, he is justified in considering that during his internship period he is *paying the equivalent of approximately fourteen dollars a day for his training and maintenance!* If the intern could keep this startling thought in mind, he might approach his daily duties more seriously, with more concentration upon their future application, and with more endeavour to make every hour count.

Relationship To Attending Staff.

Every hospital accepting interns should have a code of rules and regulations governing their duties and privileges. These should set forth clearly the place of the intern in the hospital organization. The intern must bear in mind that the patients are not his; a presumptuous intern who takes it upon himself in the middle of the night to "give 'm a quarter o' morph." (just like that) to somebody with brooding abdominal symptoms is not likely to find his consideration for his superior appreciated. "When in doubt, telephone," is a good maxim to follow at ALL times, but particularly so with reference to private and emergency patients.

If the doctor in charge cannot be located, endeavour to locate someone else with authority: the associate on the case, the chief of that particular hospital service, or, if the patient be a public patient, some attending doctor associated with that department. In case of extreme urgency, any doctor found in the building should be pressed into service, and, if visiting staff assistance cannot be obtained, or if the delay is likely to prove seriously detrimental, as in the instance of a haemorrhage or a precipitate delivery, the intern staff would be justified in handling the situation as best they can.

But no code of rules can adequately prescribe what may best be termed the "kindly spirit of the praeceptor." Fortunate, indeed, is that intern whose superiors look upon him as a junior partner—nay, as a son to whom it is a pleasure to pass on the accumulated experience of years and to coach in the complex lore of the learned leech. Many leading physicians and surgeons, looking back in later years upon their internship period, have considered their most valued and cherished memory to be that of their many informal discussions with their elders on the diverse problems of practice; their introduction to the "art" of medicine, such as the handling of recalcitrant or hysterical patients, dealing with relatives, "breaking the news," gaining the confidence of children, or the modus operandi of conducting a consultation, advice on how to get started in practice, or on how to keep office records and accounts.

And if this friendship, for so it should become, is to materialize, the intern must warrant the confidence and respect of his chief. Not only must he do his prescribed duties, but he must go to the second mile as well; the chief, being human, is perhaps none too pleased to see a new houseman, just when the former intern was beginning to be useful, but he soon begins to take a kindly interest in the newcomer, who keeps his records and work up to the minute, whose blood counts are on the chart, not somewhere in the pocket of his other coat, who doesn't always have to be called from the breakfast room to scrub, who can find a renal tumor by himself, or who is eager to conduct original investigations and to summarize and tabulate data on his own volition. The surgeon likes an intern who takes the trouble to read up the operation in advance, who knows the instru-

ments by their correct names, who knows his chief's pet method of sterilizing the umbilicus, who can anticipate every step of the operation, who doesn't pass him the scissors when he urgently needs a pair of forceps, and who doesn't invariably put the needle into the needle-holder the wrong way. He will whoop for joy to find an apprentice who is more interested in pre- and post-operative care than in getting his itching fingers around a scalpel.

No; staff appointments are very seldom indeed the result of favouritism—the usual cry of the lame duck. Not long ago, the chief of a large teaching hospital told the writer that his hardest task was to find junior men of sufficient calibre to warrant their appointment to the hospital staff! He did not insist upon brilliance so much as upon a conscientious devotion to duty, a willingness to study, and evidence of sound judgment and independent thought.

Critical Attitude Toward Medical Staff.

One feels considerable sympathy for the attending staff, for it is doubtful if there is any more critical person to please than the intern. Fresh from school, with the latest research data in his mind, he is very prone to feel disdain for the time-honoured technique and the diagnostic methods of yesterday. Filled with enthusiasm for certain theories or methods, he finds it difficult to appreciate merit in other opinions, and only when repeated observation proves to him that excellent results can be accomplished by widely opposed approaches does his viewpoint broaden. Herein lies one advantage of including in the intern staff graduates of various medical colleges.

When the hospital is an "open," non-teaching hospital, with every doctor in the community a member of the staff, and, in many instances, privileged to do his own public ward work, the intern is very likely to be critical of the work of certain of the staff members—a viewpoint which occasionally may have some justification, and which may be freely expressed before the interns by the better trained members of the staff. It has been opined that contact with slipshod surgical technique, or with inadequate diagnostic studies, may undo much of the scientific grounding so carefully instilled at college; perhaps this is true, but the utilmate effect, good or evil, depends upon the intern himself. The chief of one obstetrical service, when his intern commented upon the utter disregard of the principles of technique manifested by several practitioners conducting cases in that department, replied: "My dear boy, an internship should teach you not only how to practice medicine, but how NOT to practice it!"

However, while certain staff members may not fully utilize modern methods, the intern should be the last to criticize his superiors. What some practitioners may lack in laboratory grounding they more than make up in clinical experience; and they have a clinical judgment founded upon years of training of the eyes, the fingers, the ears and even the nose, which all the test tubes in Christendom could not produce. The best clinical judgment results from combined bedside observation and laboratory study; the medical school rightly emphasizes the latter (although it does not neglect the former), largely because if the student does not get a laboratory training at college he will never get it; therefore the intern should miss no opportunity of picking up the least crumb of bedside wisdom.

Relationship To Superintendent And Nurses.

Because of the intern's responsibility professionally to the medical staff, his relationship to the other members of the hospital family may not be clear. It should be borne in mind that in matters of discipline he is responsible to the superintendent, by whom, as a rule, he is appointed. With respect to the nursing staff the relationship is

not so clearly defined. When carrying out the instructions of the visiting staff or when doing dressings, the nurses follow his directions; but the senior nurses, particularly the supervisors, cognizant of the inexperience of the junior interns, are prone to use their own judgment in many matters—and rightly so, too, for interns are apt to order narcotics when simple sedatives will suffice, or order catheterization of a child when a motherly word from the nurse in the proper setting will start proceedings. The intern going on a new service would be well advised to have a frank talk with the supervisor in charge, for life is much more pleasant if she be a friend. Supervisors do not like interns who are officious, who are inconsiderate of the nurses' timetable, who spill mercurochrome on the bedding, who waste gauze, who always write "stat." but only come themselves on the third call, and who are not adept at concealing their amorous interest in certain pupil nurses.

In conclusion, keep in mind that only about 10 per cent of patients are hospitalized. Hospital experience is not parallel to that of private practice, with the possible exception of the out-patient department, which is a close reflection of office practice. The Commission on Medical Education makes this significant comment in its report: "Hospitals are concerned so largely with serious disease and surgical conditions that the intern often secures an erroneous impression of the medical needs of the community, which make him unduly reluctant to enter practice at a distance from hospital centers." Also, because most of the heads of services in large hospitals are specialists, do not gain the impression that early specialism is the only road to success. Above all, never cease to be a student, for, as reads the motto of Budaeus: "Time not given to study is lost time."

MATERNAL MORTALITY*

By R. L. NOBLE, '34.

In this paper on maternal mortality I have tried to review this broad subject in a general but fairly brief fashion, and to point out the various causes of maternal deaths, and the means of prevention which appeared to be the most reasonable and practical. The actual figures have been cut out as much as possible from the statistics, and expressed in percentages of the total maternal rate. When general statistics are quoted, the number of deaths per 1,000 living births is given. The complete public health aspect of the question is one beyond the scope of this paper, but as a reference on that problem, the recent paper in the Journal of Public Health by Dr. Van Wyck is to be recommended.

The present-day statistics from various countries in the world where reliable records are kept show a wide variation. In the period 1923 to 1927, Denmark, Norway and Finland showed the best figures with 2.6, 2.8 and 3.1 deaths per 1,000 live births respectively. England and Wales had 4.0 deaths; Germany, 5.1; New Zealand and South Africa, 4.8; Canada, 5.29; and United States, 7.3 deaths per 1,000 births. It is of interest to note that the Ontario rate in the last ten years was 5.6 deaths, while that of Toronto was 7.01 deaths per thousand. The total maternal deaths for Canada in 1931 were 1,210. The question immediately arises as to whether or not these statistics are ar-

* A paper read before the Alpha Omega Alpha Fraternity.

ranged in the same manner and are therefore directly comparable. Theoretically all these countries have adopted the international classification of maternal deaths and may be compared. Practically, however, minor differences arise which tend to alter the figures. In an investigation of the Netherlands and Scandinavia the Departmental Committee of the Ministry of Health in England found variations in the methods of assessing the maternal deaths, especially in Denmark and Sweden. They concluded that the death rate in these two countries was approximately the same as in England. The Netherlands, however, they found to have the same means of classification as in Great Britain, and undoubtedly have a lower rate. The comparison of the urban and rural rates in Canada is of some importance. During the last ten years there has been a steady increase in the death rate in cities and towns of over 5,000 population. In 1922 the rural rate was 4.41 deaths per 1,000, while the urban rate was 7.57. In Ontario, 1928, rural deaths accounted for only 33% of deaths while 67% were urban. The generally accepted explanation of the comparatively high urban rate is that the complicated country cases with a poor expectancy are hospitalized. Comparative statistics of the death rates in various hospitals and the many smaller institutions in Toronto are not readily available to the public, a fact which is criticized by some city obstetricians.

Puerperal Sepsis is the greatest cause of maternal deaths. Statistics show it to be responsible in the United States, 1927-1930, for 32.5 to 41% of deaths; Canada, 34% England, 36-38%. It is seen that these figures vary but little and average about one-third of the total deaths. This rate has remained fairly constant for the last thirty years. In the ten-year period from 1890 to 1900, the previous rate was reduced by about one-half, due to the marked advances in aseptic technique. As so little change has occurred in the last few years, a comparison of figures and methods of sixty years ago and those of to-day should give some insight into the problem of puerperal sepsis and the possible means of its further reduction. The most accurate figures I could obtain were those of Guy's Hospital, England. In the period from 1863 to 1875, with 23,591 births, the rate for total sepsis was 1.73 deaths per 1,000. In a comparable period, 1919 to 1928, with 21,423 cases, it was 0.14 deaths. In this series it is important to distinguish between spontaneous deliveries in which sepsis supervened, and cases where the infection followed major obstetrical interference, as the factors contributing to infection in these two groups are probably different. Following natural delivery, sepsis caused death in the 1863 series in 1.31 per 1,000, and in the 1919 series, in 0.046 per 1,000. In this first set of cases it was probable that trauma and direct inoculation by the hands of the attendant were not the main factors predisposing to sepsis. One factor explaining why infection was thirty times as common sixty years ago following natural deliveries was the poorly efficient system for the prevention of cross infection. Another point is that with antenatal care the general health of the mother is to-day greatly improved, and general treatment ideas are far advanced. Furthermore, in the 1860 series, deliveries were considered natural so long as they were not affected by version, forceps or craniotomy, and many cases under this heading must have been exhausted by a labour so long as to leave the patient quite unfit to deal with an infecton even of low virulence. A comparison of the death rate due to sepsis following non-spontaneous delivery shows a rate of 0.42 deaths per 1,000 in the 1860 series and 0.094 in the 1919 one. That is, a reduction of nearly five times. This is due to the fact that severe trauma is now rare, since difficult craniotomies and high forceps are avoided whenever possible by Caesarean Section or the induction of premature labour. Also the substitution of rectal examinaiions for

unnecessary vaginal exploration have undoubtedly reduced infection from an outside source. The contagiousness of puerperal sepsis was originally pointed out in some vivid papers by Oliver Wendell Holmes in 1842. His ideas, though hotly opposed by professors of the obstetrical school, whom he accused of encouraging professional homicide, are similar to those accepted to-day. Reports show that the haemolytic streptococcus Pyogenes can be isolated in over 85% of deaths due to puerperal sepsis. Only 2.7% of normal women have a similar organism in the genital tract, and usually have a normal puerperium. In most cases the organism cannot be isolated from nose, throat or gums, and does not persist on skin for any length of time. The evidence therefore supports an outside source of infection. Recent work in Scotland and elsewhere has shown that the death-rate curve due to sepsis is entirely independent from those of the other maternal causes. However, it is found to follow a curve remarkably similar in general outline to those from septicaemia, erysipelas, tonsillitis and mastoid disease. Carriers attending the parturient woman are found harbouring the virulent streptococci in their nose and throat. The use of proper sterilization, suitable antiseptics, isolation of carriers and contacts, especially those suffering from colds, are some of the means of reducing the number of sepsis cases.

The toxaemias of pregnancy are probably the second largest factor causing maternal deaths. Statistics of different countries show some variation. United States, 16-23% from this cause; Canada, 23%; England, 16-20%. This cause of death is therefore of considerable importance, especially as the majority of these deaths can be prevented by proper prenatal care. In the English series of 326 deaths from this cause, 74% had inadequate antenatal investigation. Only half of the cases ever had a urinalysis done, and in 25% of these no albumen was present. In 75% of the cases where albumen was found the treatment was deficient. Fifty per cent. of the deaths were in primiparae and about one-thrird of deaths were post-partum. The value of prenatal care will be discussed later under that heading, but it is important to note here the chief reasons given for the high death rate from toxaemias in the above series. Briefly, they are failure to estimate Blood Pressure and to maintain a careful follow-up system on the patient. Insufficient realisation of the importance of oedema as a sign of a pre-eclamptic condition, and, finally, delay in instituting adequate treatment due to not realizing the significence of warning pre-eclamptic signs. By the consideration of the above factors the mortality rate from toxaemias has been reduced well over 70% in the past sixty years in many institutions where routine prenatal care is practised. Further reduction of the present high rate should continue in the future, especially if greater care is taken in examination of cases outside the hospitals.

Haemorrhage forms the third main cause of maternal deaths. In Canada the number of deaths from this cause is about 14%; in England, 15%; United States, 12%. The number of deaths from haemorrhage should depend on the early detection of the cause, by prenatal care, and on the efficiency of the methods of combating blood loss. As prenatal care and transfusion technique have made considerable advances, the death rate from haemorrhage now should be markedly reduced. This is true to some extent. Deaths due to antepartum haemorrhage in a series of cases at Guy's Hospital sixty years ago were 0.46 per 1,000. In a comparable series to-day they were 0.28 per 1,000. This is a reduction of about one-half. It was shown that most of these deaths in the recent series were due to a toxaemia rather than the actual haemorrhage. Deaths from post-partum haemorrhage show a marked decrease to about one-sixth. This is due to the advanced methods of treating haemorrhage by transfusion. These figures,

quoted from a large hospital, show quite a favourable decrease in the death rate. The Health Committee report for the whole of England, however, shows that treatment can be vastly improved. In 204 deaths from post-partum haemorrhage, active measures to combat blood loss were conspicuous by their absence. In only 29 of these cases was intravenous saline given, and only eight received a blood transfusion. In 248 deaths from antepartum haemorrhage more than three-quarter of the patients had warning of the impending danger days or weeks beforehand, but did not go to a doctor or the hospital. The patient's ignorance of the dangers of haemorrhage, or their non-co-operation in reporting, is seen to influence the mortality from this cause.

The three main causes, sepsis, toxaemia and haemorrhage constitute about 70% of maternal deaths. Other causes less clearly defined, and with less accurate statistics, are: Accidents of Childbirth and of Pregnancy, Abortion, Embolism, Extra-Uterine Gestation, etc. Of this group, Accidents form by far the largest part. Approximately 15% of total maternal deaths in Canada are due to this cause. If all deaths entered as such *are* accidents, they should all be preventable. The rate has dropped some 9% in the last fifteen years, so it is likely that with improving technique and prenatal care this figure will continue to diminish. The probability here, however, is that many causes previously listed as accidents are entered under some other cause of death, so that the total rate will be little affected. Embolism and abortions are given as causing about 10-14% of maternal deaths in England. Most of these are preventable. The non-obstetrical causes of maternal deaths, such as heart, lung and renal disease, average only 0.3 deaths per 1,000. They therefore become a serious factor only when the rate is very low.

The causes so far discussed are seen to be those which are the direct means of death. There are many various indirect factors, however, which although not directly causing death, influence the maternal death rate. Some of the more important ones will now be reviewed. The question of obstetrical interference is one which has given rise to a great deal of disagreement amongst obstetricians, and to a burst of voluminous articles, all more or less controversial. That obstetric interference, as exemplified by Forceps, Version, Craniotomy, Caesarean Section, Manual Removal of Placenta, and Instrumental Induction of Labour, has greatly increased in the last sixty years is well known. In over 20,000 cases, 1863 to 1875, at Guy's, the total interference was in only 1.35% of the cases, while in a similar number of cases in 1928, interference was in 8.86% of cases. The use of forceps has increased over ten times. Caesarean Section and Instrumental Induction of Labour have greatly increased, as they were not practised at all sixty years ago. Manual removal of Placenta alone has markedly decreased. It is very likely that this enormous increase in obstetrical interference is not due entirely to a comparable increase in the incidence of obstetrical abnormalities. It is usually explained on the grounds of modern impatience and meddlesomeness. Writers using this line of reasoning generally conclude with the axiom: "To reduce maternal mortality—leave it to nature." Such an argument has been used so often, and when applied to indiscriminate interference is so obviously true, that one must not be carried away by its extreme application. One explanation offered for the present surgical interference is that the standards of tolerable suffering have changed as a natural consequence of social ideas. The increase in obstetrical interference has come to stay, just as improvements in living have come to stay, and the back-to-nature method is doomed. Doomed by the impossibility of forcing it on the patients rather than by any unwillingness of the obstetrician. The general outcry against interference is certainly

justified when it is excessive, but one must not expect, or cannot wish, that it should be so seldom resorted to as it was sixty years ago. The modern technique and the present-day willingness to interfere are the result of true advances in the practice of obstetrics, and with them come not an increased mortality, but a death rate reduced to one-quarter of that sixty years ago. Canadian obstetrics, fortunately, have not yet been beseiged with a marked increase of Caesarean Sections as have those of the United States. In 120 hospitals in the States, the percentage of these operations varied from 1 to 14%. In Scandinavia the percentage is 0.46. In certain German clinics it is 3.9%, and is very adversely criticized by other leading obstetricians in that country. Mortality from Caesarean Section in U.S.A. ranged from 9 to 11% of operations performed. It seems from the high incidence of this operation in certain countries that the indications for its performance are not properly observed, and the resulting high mortality is therefore avoidable.

Another problem which has a bearing on the maternal death rate, and one which is receiving considerable attention here and abroad, is the influence of social and hereditary factors. Social changes which are usually asserted to have increased the dangers of child-bearing are the relative increase in the number of primipara, with restriction in size of family; the increasing average age of all mothers primiparae and multiparae; the periodic variations in the average pelvic shape of child-bearing women. Statistics bearing out these changes are clearly seen in comparative series of 1830 and 1927. In the 1830 series, 19.5% of the women had only one child, while 24.5% had eight children or more. In the 1927 series, 55.2% had only one child, while 0.7% had eight or more. In the last ninety years a continuous and progressive change is seen in that primiparae have steadily increased, while families of four and over have decreased. The sum total of this change is generally considered to have had little effect on the maternal death rate. That this is so is that although first confinements are more dangerous, so too are those after six. That is, the risk of being a primipara is compensated for by a diminution of the risks of polypregnancies, which have decidedly decreased. The age of the primipara must next be considered. It is commonly asserted that confinements are easier and less liable to be prolonged and complicated in young primipara than in those who are older. Again, it is said that as women grow older their babies tend to become larger, with increasing dangers of childbirth. The average age of the primipara has steadily advanced in the last twenty years, from 23 years of age in 1908 to 27.5 years n 1926. The number of primipara over thirty years of age has risen 10% in the last twenty years. Those over 27 have risen 19%. It is not definitely known whether this renders the average confinement more dangerous or not, but it seems probable. It undoubtedly makes labour more difficult, and partly explains the rise in rate of use of forceps. The application of forceps in patients under and over thirty years being about 1.5 and 25% respectively. However, we have seen previously that this increased use of forceps has not raised the maternal death-rate to a very great extent, so it is probable that the increasing age of primipara has also affected it but little. With regard to changes in the shape of the pelvis, little can be said of its influence on child-bearing. In some countries, such as India, this does, with other complications, have a pronounced effect, giving a mortality rate, the highest in the world, of about 11 deaths per 1,000 births. It is possible in England and other countries, where food deprivation was frequent during the war, that its effect on the growing pelvis of children at that period may be reflected as increased difficulties in obstetrics in the future. Some general conditions often associated with a high-

er mortality rate are: Cases in rural areas which are inaccessible and often isolated from a doctor and hospital—this is especially common in large countries, such as this. Employment of married women, which prevents them attending prenatal clinics; in large cities where certain areas are overcrowded and general health is poor; also among the unemployed and poor classes, where anaemia and malnutrition are common.

The hereditary factor and that presented by the inter-breeding of various foreign races is a problem which must be taken into consideration in all new and expanding countries. Unpublished research work at the Burnside during the last five years has shown that this is probably the most important factor in increasing the material death rate. The conclusions are drawn from a comparison of statistics from primitive races of a pure descent with those found in n ew countries, a mixture of nearly all types. Amongst natives of Africa, pure Eskimos, and North American Indians, the mortality rate is well below 2 per 1,000, and the normal length of complete labour from one-half to one hour. Deaths from sepsis, haemorrhage, etc., are practically nil. Where these races have intermarried with others, the death rate is increased and labour is definitely prolonged. Each race is known to have individual pelvic shape characteristics, just as they have cranial distinctions. It seems logical that with inter-breeding these characteristics are lost, and labour becomes more difficult, with a consequent increased mortality. That this is true is supported by general statistics. Countries such as Norway, Denmark, and Sweden, with a race of people little influenced by immigration of foreigners, have a relatively low rate, whereas Canada, Australia and the United States, a mixture of all races, have the highest mortality rate. As further proof of this theory, studies here have shown that where the father and mother are alike in type and racial descent, labour is shorter and mortality less than where the parents are of opposite types.

The question of prenatal care and its effects on the maternal death-rate is a broad one, and can only be discussed briefly in this paper. Its most useful application is in connection with cases of disproportion, malpresentation, toxaemias and intercurrent disease, and complications attending them. Great reduction in the number of deaths from the above causes has been brought about by efficient prenatal care in the past sixty years. Statistics show that disproportionate deaths are now one-quarter, deaths from malpresentation and toxaemias reduced by one-half, and those due to intercurrent disease slightly less. Theoretically, the death rate from these causes could be reduced to practically zero, and in many hospitals among patients under proper care this is so. It must be borne in mind, as previously pointed out, that many cases, such as disproportion, etc., may be diagnosed by prenatal examination, and then be submitted to a Caesarean Section, which may terminate fatally, thus not altering the *total* maternal death-rate. The greatest difficulty in prenatal care seems to be that its importance is not impressed enough on doctors and their patients. The Committee of Public Health in England found that only one-half of the pregnant women in England and Wales received prenatal care, and in only 10% of all cases could it be considered adequate. The benefits derived from it can be readily seen by a comparison of statistics in any large hospital. At Guy's, for example, after routine prenatal care was adopted, the death rate fell from 4.4 deaths per 1,000 to 1.03 deaths. Despite the obvious facts of the benefits derived from proper prenatal care, the death rate from causes which should be removed by it remains relatively high. Many reasons are given for this throughout the world, and may be divided into two groups—One, where the fault lies with the doctor, and the other where the patient is the cause. In a large number of cases

collected recently in England, where faulty prenatal care was considered the main factor predisposing to their death, failure of the doctor to examine the patient was responsible in 62% of cases, while in 28% the examinations failed to detect any gross abnormality which must have been present at the time. In a series of 1,532 deaths in Canada, 1,302 had no prenatal care, or 85%. From these figures it is seen that the means of reducing the death rate by prenatal care is by impressing the importance of it on all patients, and by conducting routine examinations in an adequate and systematic fashion, the details of which should be well known. In Denmark, where prenatal care is of a high standard, great stress is laid on lectures given to women throughout the country, in which some of the possible dangers are pointed out.

The influence of the midwife on the maternal death rate does not concern this country as much as it does those in Europe, where the practice is common. Briefly, it is found in countries such as the Netherlands and Scandinavia, where the midwives are State trained and of a relatively high professional status, that deaths in their cases compare more favourably than those attended by doctors. This is to be expected, however, as the cases they attend are perfectly normal ones, and all but the simplest abnormalities are sent to a hospital to be under a doctor's care. It was found that midwives properly trained and supervised were capable of conducting normal labours. It is a method which, unless the strictest rules are observed, may be much abused with a consequent high death rate.

In a summary of the direct causes of maternal mortality there is seen a decided decrease in death rate in the last sixty years, but wth a tendency to rise in the last twenty years. The conclusion has been drawn that a great many of these deaths are preventable by various means which have been mentioned. Of the indirect causes, the intermarriage of different racial types, with the increased difficulty in labour, seems to be the main factor in raising the death rate. Increased obstetrical interference and social changes have possibly increased it slightly. Prenatal care alone has caused a marked decrease. Of these the last factor seems to be the only one which can be influenced to any extent by medical care. In England a standard for obstetrical efficiency, which is very reasonable for all types of deliveries, has been suggested. If one or more conditions laid down in this standard were not satisfied and death ensued, it was considered due to a primary avoidable factor. In a series of over 6,000 maternal deaths, a primary avoidable factor was present in 46%, and it was thought this figure would have been considerably higher had further information been procurable. In Glasgow, where a close check is kept on the records, Professor Munroe Kerr states that in 1926-1930 deaths where a primary avoidable factor was present averaged 75%. For practical purposes an average is generally taken as 50% of maternal deaths which are preventable. That such a large number of mothers should die from childbirth because their supervision and care has been faulty seems, indeed, a tragedy —a tragedy the prevention of which lies in the hands of the medical man, and one we hope to see abolished in future years.

VITAMIN DEFICIENCY DISEASES IN ADULT LIFE*

By TOSHIO KAJIYAMA, B.A., '34, and H. C. FOSTER, M.A., '34.

Experimental study of the vitamins indicates vast possibilities of their application to clinical medicine. Diets deficient in one or more of these accessory food factors have been shown to produce, not only specific diseases, but also general effects which may become of great importance in many types of ill-health. This paper will attempt to indicate what diseases occur in the adult human as a result of such deficiencies and the application of vitamins to the treatment of various ailments.

While the literature dealing with the subject of vitamins is very voluminous, and increases daily, most of the work reported is experimental, having been performed upon laboratory animals. Relatively little is concerned with actual human disease, and of this a very small fraction concerns the diseases as they occur in the adult.

Let us study these vitamins in order:

Vitamin A.

Chemically, Vitamin A is thought to be closely related to Carotene, which may be the actual precursor from which the vitamin is formed in vivo. It is found in fats of animal origin, such as milk, butter, cream, bread-fat, cod-liver oil, etc., but is believed primarily to be synthesized in the leaves and seeds of plants. It is fat-soluble.

Diets totally or partially deficient in Vitamin A have been shown to lead to the development of the disease xerophthalmia or keratomalacia. Vitamin-A-containing foods are widely distributed, and it is therefore very unlikely that many adults will suffer from such a deficiency. Hemeralopia, or night-blindness, is often associated with xerophthalmia, and is apparently the result of a mild deficiency of Vitamin A. In this form, the deficiency is represented in adults to some degree. During the war it was common among Austrian prisoners in Russia, and is apparently fairly common among Russian peasants, especially during the period of fasting before Easter, when all animal foods were forbidden. Liver and cod liver oil, eggs and the juice of carrots were used in treatment with complete success. Night-blindness is also found in Japan, occasionally appearing among Japanese railway workers in Manchuria. The disease here is related to the lack of fish in the winter months. Cures in 12-24 hours with cod liver oil have been reported. Night-blindness and keratomalacia have been reported in military camps in China. In the Dutch East Indies and also in Guatemala the disease has been found among people whose diet was abnormally restricted.

In England in 1931 there were reported 17 cases of xerophthalmia and night-blindness among 4,000 patients at one institution in the North. Cod liver oil, butter and milk, were entirely successful in treatment. In Newfoundland, a considerable amount of night-blindness is found, while xerophthalmia is practically unknown. The disease is generally found among the summer fishermen and also in pregnant women. On the fishing ships, beans and peas are the only source of Vitamin A, and the men have learned to treat themselves with cod liver or the liver of the gull or puffin.

Vitamin A deficiencies may also be produced accidentally in adults receiving artificial diets as treatment for disease. Such cases are occasionally reported. For instance, two patients receiving a diet restricted to vegetable soups, gruel and meat broth as treatment for ulcerative colitis, developed a condition similar to xerophthalmia, which promptly cleared up when the

* A paper read before the Alpha Omega Alpha Fraternity.

diet was changed. Another patient—diabetic—was found to be suffering from both xerophthalmia and beri-beri as a result of poor diet.

Deficiency of Vitamin A is also thought to produce far more widespread results in the body, among which are changes in the epithelial cells of the mucous membranes all through the body, and particularly in the respiratory tract, and also a general lowering of the resistance of the body to infection, which may be a result of the epithelial changes or as a result of changes in the immunological properties of the blood. The connection between Vitamin A and acute respiratory or other infections is, however, very indefinite, and little clinical work has been done. Mellanby and Green, the chief advocates of the theory that Vitamin A is an anti-infective principle, have tested its powers as a curative and prophylactic agent in certain infections. A few cases of puerperal septicaemia were treated with A-rich diets and an increased resistance to infection was observed. A few women were treated late in pregnancy with Vitamin A, and in these there was observed an increase in the resistance to infection after parturition over that of a similar group of untreated cases. The number of cases studied, however, was so small, that no definite conclusions should yet be drawn. Other workers have tested Vitamin A treatment in a number of cases of pneumonia with favourable results.

Various workers report frequent findings of infective conditions associated with xerophthalmia, showing a high incidence of such conditions as pneumonia, bronchitis and otitis media in patients showing xerophthalmia. Respiratory infections have been shown to be by far the commonest cause of death in populations where xerophthalmia occurs (Bombay).

Various workers report connections between Vitamin A deficiency and different conditions, such as Pernicious Anaemia, Stone in Kidney and Bladder, Adenoids, Goitre, Tumour formation and disturbances of reproductive function, but few definite results are available. It is interesting to note that in some cases of Pernicious Anaemia which showed disseminated sclerosis in the spinal cord, a watery extract of liver was effective in treatment of the blood condition with no effect on the cord lesions, whereas whole liver was of value in curing both blood and cord conditions. The added factor in whole liver may be Vitamin A, as suggested by Mellanby. Prolonged Vitamin A deficiency in adult animals has been shown to produce an aplastic condition of the bone marrow. Similar treatment has been shown by other workers to result in a reduction of the number of red cells in the blood; on giving Vitamin A there are signs of increased activity of bone marrow, but there is a long latent period before the red cells are definitely increased. If Vitamin A is now removed a second time, and then given again, a blood picture resembling that of Pernicious Anaemia is found.

Vitamin B_1.

The chemical nature of Vitamin B is uncertain, and the relations between the various members of the so-called "Vitamin B complex," i.e., B_1, B_2, etc., are not known. They probably contain some sulphur-containing compounds, however. Vitamin B_1 is water-soluble, and is found in most natural food-stuffs, especially in cereal germ, seeds, eggs, milk and meat.

Deficiency of Vitamin B_1 in the diet has long been associated with the disease Beri-beri. This occurs in two forms —(1) the "dry" type, characterized by muscular wasting, anaesthesia of skin, paralysis of the legs and other parts, and associated degeneration of the peripheral nerves; (2) the "wet" type, of which the most marked feature is oedema of the limbs and trunk with effusion into serous cavities, dilatation of right heart and congestion of liver and other viscera.

The disease occurs principally among

rice-eating populations in the Orient, but is endemic in Newfoundland and Labrador, where white wheat flour forms a large part of the diet. The disease is found in Europe when diet is restricted, as during the war, and also in Norway. During the late war it was found in Mesopotamia and the Dardanelles. Outbreaks of the disease occur from time to time in prisons, asylums and other institutions in Europe and also in North America: for instance, in 1914 an outbreak occurred in the jail at Elizabeth, N.J., caused by poor diet. It may occur accidentally in patients receiving special diets, as in the case of the diabetic mentioned before.

The onset of the disease is slow and insidious, and degenerative conditions occur which may become impossible to cure. The prophylactic rather than the therapeutic value of diet is therefore indicated in this disease.

Some of the other more general effects of B_1 deficiency are of greater interest to us. Lack of B_1 is thought is thought to lead to lack of muscle tone and weak peristaltic movements of the intestinal canal and a reduction in the secretion of digestive juices. These changes lead to loss of appetite, loss of weight, and inanition, and probably also to the development of gastro-intestinal lesions. A decreased resistance to bacterial invasion is also noticed in B deficiency. This may be a secondary result referable to the above gastro-intestinal effects. These effects are similar to those seen in other vitamin deficiencies, and will be reconsidered later in connection with balanced diets.

Vitamin B_2.

Vitamin B_2 is also water-soluble, and is found in yeast, milk, lean meat and green leaves.

Deficiency of this factor in the diet is supposed to result in the development of the disease Pellagra, but this is probably less clearly defined as a vitamin deficiency disease than any of the others.

The disease shows a wide variety of symptoms; dermatitis on exposed parts, inflammation of any part of the intestinal tract, mental disorder and lesions in the central nervous system.

The disease is found in Europe, especially during war time. A few isolated cases are found in the British Isles, and a considerable number of cases are found in the Southern States of the U.S.A. In 1927 there was a great increase in the incidence of pellagra attributed to the destruction by the Mississippi floods of the sources of dairy produce and fresh vegetables. Without going into the arguments concerning the etiology of pellagra, it appears that in the study of both pellagra and beri-beri there is room for much doubt as to the possibility that Vitamin B deficiency is the responsible factor in either case. In the case of pellagra, iron deficiency and protein deficiency have been suggested as more probable causes.

The separation of the additional components of the Vitamin B complex, B_3, B_4, B_5 and Y, have not as yet made the subject any more lucid.

Vitamin C.

Vitamin C has lately been claimed to be identical with hexuronic acid. It is found in fresh food-stuffs, fruit juices, especially lemon and orange juice, vegetables such as tomatoes, potatoes and raw cabbage leaves.

The relation between Vitamin C deficiency and the development of scurvy is well known. This relation is more clearly defined than in many of the other vitamin deficiencies and the dramatic nature of the cure of scurvy by administration of fruit juices is well known.

Typical scurvy is very rare nowadays because its cause is familiar to those whom it might affect. The chief features of the disease are gingivitis, haemorrhagic and painful swellings of the joints, petechial haemorrhages of the skin and anaemia. Partial deficiency results in a mild form of the disease characterized by fatigue, drowsi-

ness, depression, irritability, palpitations and loss of appetite developing haemorrhages, pains in the limbs, swollen gums and intestinal disturbances.

Scurvy has been found occasionally in Western Europe and in North America in isolated cases, due to poor living conditions or curious food habits. In Newfoundland and Labrador cases still occur. Occasionally outbreaks occur among soldiers in warfare and in prisons.

Vitamin C deficiency may be met with more often in its milder and more general manifestations. Disturbances in metabolism have been shown to occur with this deficiency, the changes presumably being responsible for the symptoms of scurvy. Iron metabolism is apparently upset; the reserves of organic iron in the liver tend to become exhausted when the diet is deficient in Vitamin C. Metabolism of other minerals, nitrogen, carbohydrate and cholesterol metabolism have all been shown to have been affected, the exact nature of the changes being, however, still very obscure. Defective calcification of the bones in the young is one of the signs of scurvy due to deficiency of Vitamin C. This may indicate the importance of the presence of adequate C in the diet in the healing of fractures. Lowered resistance to infection and to toxic substances also is said to occur as a result of deficiency of Vitamin C. Scurvy has also a bad influence on the healing of wounds. Vitamin C, apparently, promoting the rate of regeneration of damaged tissue.

Vitamin D.

Vitamin D is apparently closely related to ergosterol, being formed when ergosterol is irradiated with ultra-violet rays. It is fat-soluble, and its sources are somewhat similar to those of Vitamin A, being found in animal fat, vegetable oil, cod liver oil, etc. It is believed to be synthesized in the skin through irradiation by the rays of the sun.

The typical result of deficiency of Vitamin D in the diet of children is Rickets, characterized by imperfect calcification of the bones. In the adult a somewhat similar disease — Osteomalacia—is found, also characterized by bone changes and a loss of Calcium from the body. Many cases of this disease occur in India, China and the Balkans, particularly among women who are confined indoors. In Vienna, in 1919-20, an attack broke out among the poorer classes. In England, Northern Europe and North America occasional cases are met with, usually in pregnant women, but also in girls at puberty.

Physiologically, Vitamin D is intimately connected with the metabolism of Calcium. In cases of infantile rickets and also in adult osteomalacia, tetany is found, and the use of Vitamin D in the cure of tetany is suggested. This use has been tried with success in Toronto in cases of adult parathyroid tetany. The value of Vitamin D in promoting healing of fractures and the proper development of sound teeth in children is well known, and it is likely that the same conditions in the adult will be affected by the amount of Vitamin D available. In Tuberculosis, Vitamin D may possibly be of value in promoting healing of the lesions by calcification of those lesions.

Vitamin D has also been shown by various workers to be of value in such diverse ways as increasing resistance to bacterial and parasitic infection, improvement of progressive muscular atrophy, dementai precox, development of the embryo, some gynecological disorders, pernicious anaemia, radiation sickness, and in retarded blood coagulation and dressings for wounds.

An interesting feature of Vitamin D lies in the effects of over-dosage of the vitamin. A great excess of D in the diet (20-50 times the normal amount) has been shown to produce harmful effects, such as toxic conditions, loss in weight, vomiting and renal damage, hypercalcaemia and disposition of calcium in many organs of the body. These effects may partly be due to the toxi-

city of cod liver oil, but many of the changes also take place with excessive doses of irradiated ergosterol.

Vitamin E.

Vitamin E is a fat soluble factor probably lipoid in nature. It is found in practically all foods, more particularly in wheat embryo seeds, green leaves and milk fat.

In the female, lack of Vitamin E leads to sterility in a peculiar manner. Gestation occurs normally, but after a certain length of time the developing foetus is re-absorbed. The condition may be cured by giving foods containing Vitamin E before or even after gestation has begun.

In the male, the deficiency leads to degeneration of the testicular epithelium and is not always curable.

Clinically, the vitamin appears to be of little importance, its occurrence in food being so universal as to render its deficiency almost impossible. Some records exist, however, of its use. In two patients who had experienced four and five previous miscarriages, treatment with wheat germ oil resulted in a successful pregnancy in each case.

* * * * *

In addition to the specific deficiency effects of individual vitamins, there appears to be reasons for attributing many clinical conditions to faulty nutrition, in which one or more vitamins play an important role.

In some cases of intestinal disturbance, where loss of tone of large bowel with decrease or absence of haustral markings and increased length are found, diets low in carbohydrate and high in vitamins, particularly Vitamin B, resulted in marked improvement. The same diet proved of value in many cases of chronic arthritis, being most beneficial in those patients who also showed colon disturbances, and in which the development of arthritis was probably secondary to or influenced by the intestinal disturbance. The amount of carbohydrate in the diet has been shown to influence the ease with which vitamin deficiency diseases of some types may be produced.

Some degree of anti-infective power has been claimed for almost all of the vitamins. In this respect Vitamin A appears to lead in popularity, and yet it may be that resistance to infection is lowered by general malnutrition, if any one factor of the normal diet is omitted, rather than by specific vitamin deficiency. McCarrison points out that lack of Vitamins A, B and D may bring about an alteration in the distribution of bacterial life in the lumen of the gastro-intestinal tract. In this way, and aided by the stasis and lack of gut tone that occurs, bacteria remain visible for some time, the flora of the large intestine may extend up into the small intestine, and there is brought about a gradual and progressive loss of power of body surface to control their attack. Various infective conditions have been treated with vitamins with rather indefinite results. In addition to the examples already quoted, the following may be mentioned:

In Tuberculosis, diets containing liberal amounts of all vitamins were administered to a group of patients, with the result that one-third of the group showed favourable results attributable to the diet. In another case, administration of cod liver oil and tomato juice, containing Vitamins A, B, C and D, resulted in improved healing of intestinal tuberculosis lesions.

In pyorrhea alveolaris and dental caries, Vitamins A, C and D appear to play a large part, more particularly at the stage when teeth are developing, but probably also in adult life. Thus, Vitamin A is responsible for the conditions of the soft tissues about the teeth, D for the normal calcification of the alveolar bone and other hard tissues. Vitamin C is probably also responsible for the condition of the gums, and also, it is claimed, for the actual structure of the teeth.

In the treatment of Graves' Disease, a mixture of Vitamins A and D and

an iodo-fatty acid has been shown to be superior to Lugol's solution.

It has been suggested that Pernicious Anaemia may be a mixed vitamin deficiency disease; underfeeding of Vitamin A over a long period of time being responsible for the blood and gastro-intestinal changes; deficiency of B for the nervous conditions, and partial or complete absence of C being responsible for the haemorrhagic tendency.

It is almost unnecessary to add that the pregnant woman and the nursing mother require liberal supplies of vitamin sources in their diet, both to meet the requirements of the developing child and fo rtheir own needs. These latter are in particular the fat-soluble vitamins, A to prevent infection, and D to prevent the development of bone changes. It must be noted that the pregnant woman tends to use up her body reserves of fat and consequently her reserves of these vitamins, on which she may be depending.

Conclusions.

1. The classical types of vitamin deficiency diseases may occur in the adult. They are usually amenable to treatment by vitamin feeding.
2. Vitamin deficiency may accidentally occur as a result of the use of special diets in treatment, and care should be taken that such diets contain all vitamins.
3. The use of vitamins in medicine should be as a prophylactic measure, in which better effects are shown than in the cure of disease.
4. The pregnant woman and nursing mother in particular require special attention to their vitamin needs.

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THEY WERE ALL WRONG

WILLIAM PITT said "There is scarcely anything around us but ruin and despair."

WILBERFORCE in the early 1800's said, "I dare not marry, the future is so dark and unsettled."

LORD GREY in 1819 " . . believed everything was tending to a convulsion."

THE DUKE OF WELLINGTON on the eve of his death (1851) thanked God he would " . . be spared from seeing the consummation of ruin that is gathering around us."

DISRAELI (1849), "In Industry, Commerce and Agriculture there is no hope."

QUEEN ADELAIDE said she ". . had only one desire, to play the part of Marie Antoinette with bravery in the revolution that was coming on England."

LORD SHAFTESBURY (1848), "Nothing can save the British Empire from shipwreck."

WE CAME THROUGH ALL RIGHT THEN — AND SHALL DO SO AGAIN

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THE SECRETION OF HYDROCHLORIC ACID

By LAURENCE IRVING, Ph.D. (Stan.),
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The secretion of the gastric mucosa is unique in containing about 0.5 per cent. hydrochloric acid. No other tissue could withstand continuous exposure to an acid solution of that strength and, in fact, it appears that the mucosa itself occasionally succumbs to its own secretion under abnormal circumstances. It is a dangerous reagent, and may be as potent for causing harm in disorder as it is essential for promoting digestion under proper conditions.

The principal characteristics of the secretion of hydrochloric acid present a physiological problem of apparent simplicity. The acid is secreted by the parietal cells of the fundic mucosa. In the pure juice of the digestive secretion there is a definite concentration of about normal acid with pH slightly less than one. The only possible source of the hydrochloric acid is in the blood chlorides, and as chloride ions are removed from the blood they are replaced by bicarbonate ions. Evidently the mucosa is to be regarded as a mechanism which can separate hydrochloric acid from neutral blood chlorides and substitute bicarbonates. If we represent the process by a formula,

$$Na\ Cl + H_2CO_3 = Na\ HCO_3 + HCl$$

but the formula indicates only the net results and presents no implication as to how the reaction is accomplished.

The separation is effected by the secretory activity of the parietal cells, and it might be expected that during the secretion of strong acids the cells themselves would show an increased acidity. By examining the alkali reserve of secreting and non-secreting mucosa, we found that it was neither acid nor alkaline at any time, but approximately neutral, like any other tissue. There is no displacement of the acidity of the mucosa either by the accumulation of products or secretion before they are discharged into the lumina of the glands, nor afterward by any subsequent re-absorption of the secreted acid.

It might be suspected that the ability of the cells of the mucosa to withstand exposure to the strong acid without change in their own acidity depended upon the possession of a considerable buffering ability. However, when we examined the buffering power of the mucosa by titrating it with carbonic and other acids, we found that it was similar in this respect to other tissues, and rather less well buffered than blood. The mucosa is not shielded from the acid which it secretes by any special buffering capacity, and the survival of the cells in contact with the strong acid is due to the failure of secreted acid to penetrate, and not to any peculiar internal properties.

An ingenious suggestion has frequently been offered which would allow for the secretion of acid without injury to the cells during its passage through them. The proposition is that a neutral chloride, perhaps an organic compound, is secreted, and that after its discharge an enzyme decomposes the substance in the lumen of the glands. But no such substance or enzyme has been discovered, nor is it reasonable to expect. The separation of hydrochloric acid from a neutral chloride can only be accomplished by the application of a considerable amount of energy, equivalent to that which is used in the decomposition of sodium chloride by electrolysis. While the metabolism of the cell could afford the requisite energy, it is improbable that the cellular mechanism could project that force beyond its own cell walls in order to accomplish the separation of a neutral chloride in the lumen.

The same considerations apply to the formation of hydrochloric acid within the parietal cells. It is quite immaterial what mechanism is postulated for the formation of hydrochloric acid, whether it be by an easily observed process of electrolysis, or by some device as yet unknown, which is operated by the cell. In forming strong acid from a neutral solution, the cell or any other mechanism must apply energy to the extent of the energy which could be derived from the neutralization of the strong acid.

It is known, in fact, that other cells can perform acts of secretion in which chemical and physical energy are required, and that their metabolic processes are such as to afford the requisite amount. We have also had an indication as to the nature of the metabolic processes which maintain the mucosa, derived from a study of the development of acid in the dying tissue. As the tissue dies, it becomes more acid—not to a degree which indicates that the secretion of hydrochloric acid is proceeding postmortally, but in a way that resembles the postmortal changes which occur in muscle. In muscle the development of postmortal acidity follows from the formation of lactic acid, which in life is supplied to the support of muscular activity. The postmortal process represents the perversion of the normal reaction when all vital directing restraints have been removed, but it nevertheless reveals one of the vital reactions. So the fact that the mucosa develops acid postmortally in a manner characteristic of the better-known muscular tissue suggests that a similar kind of metabolic process supports the activity of the mucosa.

With the aid of these observations we can now reconsider the process of secretion of hydrochloric acid and slightly clarify the view. The chloride ion of the hydrochloric acid is derived from the sodium chloride of the blood, and in the process of secretion the acid is directed into the lumina of the glands by the secreting cells, while sodium bicarbonate is transported into the blood. For each molecule of hydrochloric acid formed, one molecule of alkaline sodium bicarbonate is produced, and the presence of equal amounts of acids and alkaline substance would not affect the neutrality of he parietal cells. Apparently it is not necessary to look for the development of acidity in the mucosa, for acid secretion is only half of the process, and the other half is the secretion of base. As a consequence we should regard as the function of the parietal cells the direction of a stream of hydrochloric acid toward the lumen of the gland, and of a corresponding amount of alkali in the form of bicarbonate toward the blood. The separation of a neutral chloride can only be performed by the expenditure of energy. The energy is derived from the metabolism of the cells, and we have even suggested a metabolic process.

We might inquire whether any of the inorganic membrane systems would furnish an analogy for gastric secretion. But none of the inorganic systems furnish the proper model, for they depend upon an osmotic distribution leading to an equilibrium. There is nothing in a secretion process which suggests analogy to the membrane equilibrium systems which are known, and the facts of secretion indicate that the process proceeds to break down the ordinary equilibrium situations by the selective transport of specific components. When secreted substances are electrolytes it is to be expected that electrical changes should accompany secretion. An electrical potential difference has, in fact, been measured in the mucosa, and while it does not reveal the mechanism of secretion, it may be regarded as another sign of the expenditure of energy in the process.

It may appear that I have given undue prominence to a few observations in attempting to describe the process of acid secretion. Whoever is familiar with the subject will recognize that the scheme of secretion which I have proposed was based upon the sum of the

experience of many observers, and that I have simply used my own observations to point a critical examination at the progress of our knowledge of secretion. There are still many complications in our view of the process, but we are advancing toward a simpler statement of the facts. It is high time that the physiological view of the subject should improve, for the observations of some acute clinicians are directing our attention to the specific relation of hydrochloric acid secretion to certain definite manifestations of disease.

THREE CASES OF PERFORATED DUODENAL ULCER

By W. J. VIRGIN, '33.

Introduction.

Peptic ulcer is a condition met with in both medical and surgical practices. It may be defined as a condition due to digestion of a portion of the wall of the stomach or duodenum by gastric juices; the digestion occurring in an area of lowered vitality. There are several theories as to the cause of peptic ulcer, but the two fundamental requisites appear to be a site of lowered vitality and the acid secretion of the stomach. The ulcers may be acute or chronic, and all stages of inflammatory reactions are found in them. The acute varieties tend to be superficial and confined to the mucosa. They occur most frequently in females. The chronic varieties are much more numerous in males than in females—about 4 to 1. They penetrate to the muscle layer and may involve the serosa. Adhesions to neighbouring organs with penetration into their substance may occur. The major complications of peptic ulcers are perforation, haemorrhage and cicatrization. The cases presented in this paper demonstrate the complication of perforation in duodenal ulcer, but haemorrhage and cicatrization are also shown. Duodenal ulcers are found more frequently in Canada than gastric ulcers in a ratio of 4.7 to 1. Without complications, they are relatively less serious than gastric ulcers, but here we wish to discuss the condition with perforation.

Case Histories.

Case 1.—W. J., age 37; married; linesman for Hydro.

Complaint.—Severe epigastric pain, nausea and vomiting, five hours.

History.—For the past four years the patient has suffered from attacks of pain in the epigastrium related to meals. Pain occurred one to two hours after eating. It did not radiate, but caused discomfort to the right of the mid-line. It was relieved by taking soda or food. The attacks lasted three or four weeks and the patient felt well between them. His appetite was good. Suddenly, at 7 p.m. one evening, he was seized with a violent stabbing pain in the epigastrium which doubled him up. The pain decreased, then became more severe, so that he was scarcely able to walk. He was taken to hospital at 11 p.m. By this time the pain had increased in extent. It was steady and severe.

Physical examination.—The patient was strong, well developed, white male. He lay flat on his back, motionless, apparently not daring to move. He groaned with pain frequently. His respirations were shallow.

The abdomen was flat and did not move with respiration. On palpation the upper abdomen was rigid and board-

like. There was marked tenderness in the R.U.Q. just above the umbilicus near the right costal margin. Rebound tenderness was present. The percussion note in the upper abdomen was tympanitic. Liver dulness was not decreased.

Operation.—The perforation was found on the antero-superior aspect of the duodenum within one inch of the pyloric vein. The wall of the duodenum was inflamed and thickened. The peritoneum was thickened about the perforation.

Case II.—A.B., age 32; married; truck driver; no work for one year.

Complaint.—Severe epigastric pain.

History.—The patient has had epigastric distress for three years. At first he complained of gas between meals with pain when hungry. Later he vomited his food and obtained some relief. The pain increased in severity and pierced through to his back. It was relieved by food or soda. He has been treated for duodenal ulcer for the past year. Some improvement was noted, but lately the attacks have been more severe.

At 8.30 a.m. the patient was seized with an attack of severe epigastric pain khile in bed. He took milk and soda for relief but vomited it. He was admitted to hospital at noon.

Physical examination.—The patient was a young male adult. He was well developed in appearance. He lay quietly on his back in bed, not greatly distressed. There was a slight epigastric movement with respiration. The R.U.Q. was tender and somewhat rigid. The epigastrium was tympanitic. Liver dulness was not decreased.

Operation.—The perforation was found on the anterior wall of the first part of the duodenum. The wall was thickened and indurated. The gut was constricted at the site of ulceration.

Case III.—N.F., age 36; married; butcher by trade.

Complaint.—Acute pain in the abdomen, ten hours.

History.—The patient has had trouble with his stomach since childhood. He suffered from bouts of epigastric pain with vomiting one to two hours after meals. The pain was relieved by food or soda.

At 10 a.m. the patient was seized with a severe attack of epigastric pain which was increased by movement. He remained at work until noon, and was then brought to hospital.

Physical examination.—The patient was a rather thin white male. His muscular development was only fair. The abdomen was scaphoid, and moved slightly with respiration. There was marked tenderness in the R.U.Q. with a point of maximum tenderness to the right of the mid line on a level with the umbilicus. Some tenderness was noted on the right side per rectum.

Operation.—A perforation was found on the anterior wall of the duodenum, one-half an inch from the pyloric vein. Thickening of the wall was noted.

Discussion.

Perforation of a duodenal ulcer as illustrated by these cases is of importance. It may be considered under the following heads:

1. *Age incidence.*—The accident has occurred in young individuals in the prime of life. The usual age for doudenal ulcer lies between 30 and 45 years. Hence though not common, one must be prepared to meet this complication in people of an age when invalidism is very undesirable.

2. *Previous history and findings at operation.*—In each instance there is a history indicative of duodenal ulcer which goes back for a period of years. Again at operation the sites of perforation were indurated and showed serosal involvement. These two considerations help to demonstrate that perforation tends to occur in chronic ulcers though it also occurs in acute ones.

3. *Type of individual and the risk involved.*—The fact that two of the perforations occurred in healthy, active, married men who had relatively little

illness of serious import is significant. The accident meant that these persons were faced with an abdominal catastrophe with a very high mortality apart from surgical intervention. The time elapsing between the perforation and operation alters the outlook for such patients materially. One set of figures is as follows: The mortality with operation within 12 hours of onset is 6.5%; within 24 hours 20%; after 24 hours 66.6%.

Cases I. and II. were both strong, healthy individuals and both were operated upon within 6 hours of the onset. They made a rapid recovery and suffered little during convalescence.

In contrast to these, the remaining individual has had gastro-intestinal trouble from childhood. He is not robust and suffered accordingly. Following operation he progressed fairly well for 8 days, though he could not tolerate food. On the 9th day he began to show evidence of haemorrhage.

Two transfusions of 300 cc's each on the 10th and 11th days did not raise the haemoglobin above 25%. In this case the complication of haemorrhage has made the prognosis grave, although all signs of peritonitis have vanished.

Treatment.

Operation. — Operation was undertaken as soon after admission as possible. Morphine gr. 1/4 and Atrophine gr. 1/150 were given on the ward. Spinal anaesthesia was used in all cases. The incisions were made near the midline over the upper part of the right rectus and the perforations were found. They were surrounded by purse-string sutures and invaginated as the sutures were tightened. Pieces of omentum were stitched over the sites as an additional precaution. In case No. 2 a posterior gastro-enterostomy was performed on account of the constriction. Drainage was instituted.

Post Operative Treatment.

(a) Shock, dehydration and accidosis—1000 cc's of 5% glucose in saline was given intravenously after operation. 2000 cc's of glucose solution were given on the 2nd and 3rd days also.

(b) Pain—morphia gr. 1/6 or 1/4 P.R.N.

(c) Sleeplessness—luminal, codeine.

(d) Position—semi-Fowler's.

(e) Distension — enemata P.R.N.; Serine and Pituitrin; linseed poultices to abdomen.

(f) Diet—nothing by mouth for 3 days except sips of water—1 ounce of water every hour on 2nd and 3rd days. On the fourth day small amounts of gruel. This was increased gradually and soft articles of diet were added up to 14 days.

(g) 25 cc's of B. Welchii serum were given on the day after operation.

The treatment of these cases should not cease with convalescence from operation. Living habits should be investigated and corrected where necessary. A suitable diet should be arranged and a proper amount of rest prescribed. These patients should be kept under observation for one or two years after operation. If these details are attended to, then there will be reason to anticipate a cure of the condition which resulted in the original accident.

THE PHYSIOLOGY OF THE CORONARY CIRCULATION*

By D. Y. SOLANDT, M.A., '33.

The mammalian body depends on the adequacy of the coronary blood vessels as it depends on no other part of the circulatory system save the vascular supply to the vital centres in the brain. In view of this undeniable importance, it is somewhat surprising that the coronary vessels almost completely escaped the attention of early workers in the fields of anatomy and physiology.

Although the existence of the coronary vessels was recognised at a much earlier date, the first account of research in this field was published by Baptista Scaramucci in 1689. There was a great deal of speculative interest at this time in the exact role and importance of the coronary blood vessels and Scaramucci raised a great deal of controversy when he made the almost inspired statement that the intramuscular coronary arteries emptied during the contraction of the heart muscles and filled while the heart was relaxed. This was pure hypothesis at the time, lacking as it did any experimental evidence, and as such was vigorously attacked by Stroem in 1707. Stroem maintained that the reason for the lack of filling of the coronary vessels during systole was that the mouths of the coronaries were occupied by the semilunar valve flaps at this time in the heart cycle. Such a view was far from unreasonable and was given general credence until late in the last century. In 1899 Langendorff published the results of careful experimental work on what we call the mechanical control, more properly the hydraulics, of the coronary circulation. Langendorff's conclusions almost voice the modern views on this subject and his experimental methods are still used for investigation in this field. We may consider Langendorff as contemporary with present-day authorities in the realm of coronary physiology. His work marks the beginning of the present era in investigative approach to the problems of this subject.

*Paper presented at Alpha Omega Alpha Honour Medical Fraternity Meeting, Jan. 23, 1933.

SOME ANATOMICAL POINTS.

Before broaching the study of the modern views on the physiology, let us consider a few of the more important anatomical features of the coronary circulation.

The blood demands of the heart musculature are met through the agency of the two coronary arteries. The right coronary artery arises from the aorta slightly below the level of the right anterior aortic cusp and runs to the right in the auriculo-ventricular sulcus, where it ends in two smaller branches. The left coronary artery gains its origin from the aorta in the left anterior sinus of Valsalva and, running forward and to the left, bifurcates to form its two main branches. Of these the circumflex runs to the left and the descendens passes down in the anterior interventricular sulcus towards and to the apex. The blood from the heart is returned chiefly to its own right auricle. This is accomplished by venous channels of which the largest is the coronary sinus. Blood is also returned to all the cavities of the heart by the Thebesian veins which, according to Grant and Viko, can be found perforating the endocardium in any region.

The question of the anastomoses of coronary vessels remained a point of contention for many years. The work of Louis Gross proved that the old conception of coronary arteries as essen-

tially end vessels was quite false. Using special methods for injecting the vessels, Gross has shown that abundant anastomoses exist and that the older the heart the more profuse are the anastomotic connections. Venous anastomoses are also plentiful and, due to their action, efficient drainage is possible even in the face of complete occlusion of the coronary sinus; this has been experimentally proven by Grant and Jones.

The work of Gross has brought forth another interesting point in the fact that in foetal life the right side of the heart is the more abundantly supplied with vessels. During the first decade the two sides seem to have about the same extent of vascularity. In adult life the vascularity of the left side increases and that of the right decreases, the anastomoses between the two sides, however, being greatly increased over what is found during childhood.

The coronary vessels themselves, quite apart from their distribution, have received a great deal of attention. Walkoff found differences in the structure of the large and small coronary arteries which did not correspond with the histological findings in other arteries of similar lumina. The chief difference noted was a marked intimal thickening in the larger vessels, and this was found present from earliest years. The most recent work on this subject, reported by Spalteholz and Hochrein in 1931, verifies Walkoff's work and suggests that this intimal thickening is for the purpose of damping changes in pressure. These workers also claim that the coronaries are much less dilatable than the aorta and they find that the longitudinal musculature of these vessels has a peculiar function to perform in adapting the vessels to changes in form of the organ. In their physiological findings these workers are diametrically opposed to contemporary authorities in this realm of research.

MODERN VIEWS ON THE PHYSIOLOGY OF CORONARY CIRCULATION.

Work on the investigation of the coronary circulation from a physiological standpoint has so-far dealt almost entirely with the regulation of the blood flow in this vascular system. We will confine ourselves fairly closely to the problem of this regulation and, rather than discuss experimental methods and detailed results, we will consider chiefly experimentally derived conclusions and the basic principles that they indicate. Our aim will be a comprehensive understanding rather than an unwieldy body of facts.

The study of the regulation of the coronary circulation divides itself naturally into a consideration of the various mechanisms entering into the maintenance of this regulation. These

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mechanisms are essentially either mechanical, chemical, or neurological and may be conveniently examined in such groups. Let us first consider the factors involved in the mechanical regulation of conorary circulation.

Mechanical Regulation.

Among the modern investigators in this branch of the work, Anrep and his school are outstanding. Following Evans and Starling, they attempted to discover the effect of the various physical forces that may normally alter the coronary blood flow. As an aid to this investigation, they determined the percent of blood drained by the coronary sinus and found this to be three-fifths of the total coronary flow. This value was found to be constant under all circulatory conditions and could be used as a measure of the total flow. These researches indicated another interesting fact in that the left coronary artery was found to carry 80 to 85 per cent. of the total coronary flow. Although this value was constant in the experiments performed, the anatomical work of Gross would lead us to believe that a certain marked variation would be expected with age.

Investigating the coronary flow with relation to the phases of the cardiac cycle, Anrep verified much of the earlier of Porter and Pangendorff. It is readily appreciated that the haemodynamics of the coronary blood flow are complicated by the rythmic contraction of the myocardium, within which all the smaller vessels lie, and also by the rapid and extensive changes in pressure which occur in the chambers of the heart. We may consider it a well established physiological fact that the coronary inflow rises during diastole to reach its peak just at the beginning of systole. The onset of systole causes a rapid fall in coronary flow. Anrep, Davis and Volhard in 1931 published the results of work which they believe indicates that the coronary arterial flow comes to a standstill and in many cases actually reverses during systole. Perfusing by the normal pulsating aortic pressure, these workers found that the blood in the large coronary vessels moved forward during two phases of the cardiac cycle. The main movement occurs as we have indicated, during diastole, and this is followed by a second very transitory forward movement at the commencement of systole. The second movement does not represent true coronary blood flow, but is rather a measure of the elasticity of the large coronary vessels. Such a transitory movement can be produced by increasing the aortic pressure, even in the face of complete occulusion by myocardial pressure at the arterioles and capillaries. The mechanical regulation of flow in the right conorary artery has not received much attention from experimental physiologists. The pulmonary pressure is approximately one-fifth that of the systemic arterial pressure and for this reason it is logical to suppose that the blood flow in the right coronary artery is but little effected by the systolic contraction of the heart.

Coronary outflow fairly accurately mirrors the inflow. That is, the main ejection of the blood from the venous side of the coronary circulation takes place during systole and is chiefly due to the myocardium squeezing the thin-walled venous structures. Coronary outflow never reverses, but it is at a minimum during diastole. Small increases in outflow are noticed during auricular contraction and again during the period of isometric contraction, but these are quite overshadowed by the great increase in outflow during active systole.

The rate at which blood flows through the coronary circulation must depend very considerably on arterial pressure. Markwalder, later Evans and Starling, and recently Anrep, have all experimentally proved this fairly obvious fact. These experiments indicate that the coronary blood flow normally amounts to 40 to 60 c.c. per gram of heart per hour. If the arterial pres-

sure is reduced, this rate of flow is rapidly decreased and if the reduction in pressure be marked, the coronary flow will be insufficient for the needs of the myocardium, even although the reduced pressure has diminished the work that the heart must accomplish. From our remarks on the relation of coronary flow to the cardiac cycle, it is fairly obvious that the systolic pressure is not the important factor in the arterial pressure from the standpoint of coronary circulation. The important phase must occur when the aortic pressure shows its greatest height above the endocardial pressure. This is during the diastolic phase which, however, does not mean the phase of diastolic or lowest pressure. Anrep and King, using a perfused heart in which they could keep constant the diastolic, systolic or pulse pressures or the rate of coronary flow concluded that the mean aortic pressure is the important factor. However, Anrep, Davis and Volhard working more recently, have confirmed the earlier findings of Smith, Miller and Graber that it is the diastolic or, more properly, the mean arterial pressure during the diastolic phase of the heart beat, on which coronary flow chiefly depends. This is probably not strictly true in the intact animal.

Anrep, King and later Hausler, have conclusively demonstrated that heart rate, in itself, has no effect on coronary flow. However, when the rate is increased diastole is slightly shortened as compared with systole and this tends to slightly decrease the flow It has been suggested that the contractions of the rapidly beating heart are weaker than when the rate is slower, and for this reason there is a tendency towards an increase in coronary flow under such conditions This is not borne out experimentally

Chemical Regulation.

In dealing with the chemical regulation of the coronary circulation it is reasonable that we should limit ourselves to mechanisms that can and do occur normally in the mammalian body. Most of the experimental work has been done on the dog because the heart of this animal has been shown to closely resemble the human organ in both gross anatomical features and pharmacological reactions.

Chemical regulation is chiefly concerned with alterations in the calibre of the coronary vessels. As Hausler has pointed out, chemical factors may effect the coronary vessels and mask this effect by alterations produced in the systole-diastole temporal relationship. Thus adrenaline causes a dilation of the coronary vessels but, in some animals at least, systole is lengthened and the coronary blood flow decreased. Some workers get over these difficulties by taking coronary inflow during diastole as a true indication of the state of the coronary vessels. Others perform their experimental work only on the isolated coronary vessels and thus rule out the confusing factors.

The effect of hydrogen ion concentration of the perfusing blood on the coronary flow has been extensively investigated by Dale and Evans. They have found that variations in pH around the normal 7.35 to 7.40 have no effect on coronary flow. However, lowering the hydrogen ion concentration to a value between pH 7.5 and pH 7.9 does cause a marked constriction. Values below pH 6.0 have a similar effect. These results are of interest to those using artificial perfusing solutions in experimental work on the coronary circulation and help to explain much of the contradictory evidence obtained by different workers in this field.

The oxygen saturation of the coronary blood is one of the most important chemical factors in the regulation of coronary flow. It has long been recognized that asphyxia of the heart produces very large increases in coronary flow. Evans and Starling have shown that the heart muscle, under conditions of asphyxia, is able to extract oxygen almost completely from the blood. The

work of Hilton and Eicholtz indicates that the increase in coronary flow seen in asphyxia is due to coronary dilatation, and that this is entirely proportional to the degree of deoxygenation of the arterial blood. Apparently this is a mechanism concerned with supplying the heart with the necessary oxygen under the most adverse conditions of blood desaturation. Garry has shown that plain muscle in general is relaxed by oxygen lack, and this, in part at least, explains the action of the coronary vessels.

Tissue metabolites collecting in the tissues themselves, or in the blood stream, and also the carbon dioxide content of the circulating blood, have been suggested as the real factors underlying the changes apparently due to oxygen want. Experimental evidence, however, shows that these factors, when independently varied, have but little effect on the coronary blood flow.

Adrenaline shares with oxygen the place of major importance in the chemical regulation of the coronary circulation. This hormone constricts the systemic and the large coronary arteries but dilates the small coronary vessels. As we have mentioned, the effect on the length of systole may mask the dilatation if the amount of the hormone is small. It is of interest to note that ergotoxin abolishes the constrictor effect on the large coronaries but not the dilator effect on the small branches.

The effect of histamine on the coronary circulation depends on the particular species with which we are dealing. Cruickshanks and Cubba Rau reported experiments in which they had verified the findings of earlier workers to the effect that histamine constricts the coronary vessels in he dog, ox and man, and dilates the same vessels in the cat. Histamine, in fairly large doses, increases the force and rate of the heart beat in many species, but this cannot be directly attributed to any changes produced in the coronary circulation.

Neurological Regulation.

The majority of the foregoing observations on the mechanical and chemical factors controlling coronary blood flow are based on experimental evidence obtained with denervated preparations. In the intact animal, the nervous elements of control play a major role and must be considered if a composite picture of the integrated mechanisms is to be attained.

Contrary to the earlier findings of Evans and Starling, Woollard and his co-workers have found that the coronary arteries are richly innervated down to their finest ramifications from both the sympathetic and parasympathetic systems. The vagus furnishes the chief nerve supply to the smallest vessels, whereas the larger vessels derive nerve fibres almost equally from both components of the autonomic nervous system.

Anrep and Segall have recently confirmed Wigger's original contention that the vagus carries constrictor fibres to the coronary blood vessels. These workers showed that the vagus normally carries tonic constrictor impulses to the coronary vessels. Cutting the vagus produces a dilatation of the coronary arteries which is quite independent of the increase in heart rate. Section of the vagus produces an increase in coronary flow even when atropine has been administered to prevent any change in heart rate. The action of the vagal impulses on the coronary arteries would seem to be quite separate from the action on the heart proper, although the two actions obviously fit together from the functional standpoint.

We have seen that, in the denervated preparation, increased systolic output often actually decreases the coronary flow. Anrep and Segall, working on innervated hearts, have shown that there is what might be called a coronary component to the Bainbridge reflex by which increased cardiac output causes a relaxation of coronary tone and a resulting increase in coronary

flow. This effect disappears on section of the vagus nerve.

The effect of the sympathetic supply to the coronary areries is neither so evident nor so thoroughly investigated as the vagal action. The administration of adrenaline or the stimulation of the stellate ganglion produces a marked vaso-dilatation, and investigators claim that this is chiefly confined to the smaller branches of the coronary system. Severe sensory stimulation or cerebral anaemia will cause a dilatation of the coronary arteries, which only occurs if the sympathetic pathway through the stellate ganglion remains intact. The recent work of Stella on the carotid sinus and its relation to coronary flow would seem to indicate that, in altering heart rate as part of the mechanism in compensating for changes in cerebral blood pressure, the coronary flow is correspondingly changed. Apparently further work is required to discover the pathways by of coronary flow rests chiefly in the oxygen saturation of the arterial blood.

Führer, Starling and Straub, and later Anrep and Bulatao, noticed that an increase in peripheral arterial resistance, by raising the mean blood pressure, increased the coronary flow. Coincident with the increase in coronary flow they noted an increase in the output of both ventricles and a rise in pulmonary blood pressure. The systemic output of the heart was not increased. The explanation lies in the fact that the blood by-passed from aorta to right ventricle and thence to the pulmonary circulation is considerably increased under these conditions.

A branch of experimental investigation that has received a lot of attention lately is the electrocardiographic study of the heart under altered conditions of coronary flow. This lies more properly in the field of experimental pathology. Interesting and instructive from the physiologist's standpoint as these studies are, it would, nevertheless, be folly to add a matter of such controversy and magnitude of this discussion.

CONCLUSION.

In conclusion, it is our intriguing but dangerous task to examine the knowledge of the physiological aspects of the coronary circulation from a speculative and somewhat critical standpoint.

The mechanics of the regulation of coronary circulation have been widely investigated. Probably more is known about this than about any of the other factors involved in the regulatory function. However, the experimental methods used have come very little nearer to duplicating normal conditions than the Starling heart-lung preparation. This is considerably removed from the intact animal whose processes we are attempting to understand. The same criticism may be levelled against much of the work on the chemical factors regulating coronary flow. Studies on the isolated vessels certainly involve

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which these changes are brought about. Present data, however, indicate beyond a doubt that the control is neurological. Views on the sensory innervation of the heart are hypothetical and conflicting.

Other Aspects of the Physiology of Coronary Circulation.

So far we have dealt entirely with the regulation of the coronary circulation, and, as has been previously mentioned, this has been the most thoroughly investigated part of the field of coronary physiology. To complete the study a few other points on which recent work has been done should be mentioned.

Müller, Salomon and Zuelzer, working on the Starling heart-lung preparation, have found that the coronary flow and the efficiency of the heart muscle are independent both of the oxygen consumption of the heart and the carbon dioxide tension of the venous blood. This is in line with the findings of earlier workers, and indicates that, as regards metabolizable substances and metabolites, the control conditions far removed from the normal. Such work has its place as a stepping stone to fuller knowledge, but the tendency to attribute functions thus discovered to the normal organism is ever-present.

In studying the neurological control of the coronary circulation our present ignorance on the subject of autonomic physiology becomes at once apparent. A great deal is known concerning the end results of autonomic action, but the mechanisms by which these results are brought about are little understood. Electrical methods at present in use for the quantitative evaluation and analysis of nerve action potentials may yet do much to shed light on the fundamentals of nerve physiology. A similar approach will possibly untangle the skein of the autonomic pathways.

Viewing the question of coronary physiology as a whole, it would seem that the greatest flaw in present knowledge lies in the direction of normal functions. We know a great deal about the various mechanisms of control and very little about their integrated effect in the unmutilated animal body.

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THE FOURTEENTH INTERNATIONAL PHYSIOLOGICAL CONGRESS

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In place of the austerity of the Grecian architecture of Harvard Medical School, which had been the background for the preceding Congress, the members who assembled for the fourteenth meeting found themselves surrounded by the glories of old and new Rome. The city to-day is a splendid mixture of ancient monuments and new achievements, and is a most interesting setting for an international meeting.

After one of the hottest Sundays many of the members had ever spent—unfortunately the Congress met at the end of August—the initial meeting took place in the Hall of the Caesars on Capitol Hill. The meeting was memorable for most on account of the presence of the head of the Italian Government, who officially welcomed the visitors. It was an unique opportunity to see at close range one of the most-discussed men in the world. Following the opening ceremony, Professor A. V. Hill gave the special address on "Energy Exchanges in Muscle and Nerve."

From Tuesday morning until Saturday noon the Congress met in four sections for the presentation of papers. Readers of this Journal will be interested to know that two papers were presented by members from Toronto. Professor Best described the results of the recent work on the effects of choline on fat metabolism. Dr. Taylor discussed the influence of bile on the absorption of irradiated ergosterol. Both papers were well received and adequately discussed. A paper by a former Torontonian, Dr. Borsook, on enzyme kinetics, was also interesting.

A number of the many papers on the program were worth hearing, and several attracted particular attention. In a crowded room, Szent-Györgyi presented his statement that Vitamin C was hexuronic acid, an assumption which may or may not be correct. A symposium on sexual hormones was well attended. One presentation in that group well illustrated the facility shown by Europeans as linguists. Dr. Freud of Amsterdam gave a paper in excellent English, and fluently answered questions in French and German.

Two special addresses were given by request. Professor Karrer of Zurich reviewed the work, in which he had largely shared, on the relation between carotene and Vitamin A. At another meeting Professor Pavlov spoke on the physiology of the nervous system.

While many of the papers proved of interest, the opportunity of meeting workers in one's own field was of perhaps greater value. At an international congress the possibility of making useful contacts are numerous. For the younger members it was an opportunity to see, hear, and perhaps meet some of the most distinguished physiologists. These opportunities were made more frequent in Rome by the nature of the social events.

On the afternoon of the opening day the Congress journeyed by an electrical railway, recently built by the Italian Government, to old Ostia. The excavations were visited on foot, and the members assembled in the ancient theatre for an address on Ostia. Later tea was served in the ruins of a villa, and following tea, the journey was resumed to new Ostia, Rome's sea-shore resort.

A reception was held on Tuesday afternoon in the Palazzo dei Conservatori on Capitol Hill. This is now a museum which commemorates the ancient city, and the Congress members found

much of interest. Tea was served in the attractive gardens behind the palace. The beauty of the Italian sunset as seen from the roof of the palace that evening will long be remembered.

The official dinner was held on Wednesday evening, and on Thursday the Congress went on an excursion to Tivoli. At noon on Saturday the Congress was received by the Pope in the Throne-room of the Vatican. His Holiness spoke for twenty-five minutes. The Congress was closed on Saturday afternoon by a garden party given by Signor Marconi in the grounds of the Royal Academy of Italy.

Headed by Professor Pavlov, the Russian members presented a cordial invitation for the next Congress. This was accepted, and the Fifteenth Congress is scheduled for Moscow in the summer of 1935.

BIOPSY IN MAMMARY CANCER*

By JAMES EWING, M.D.

The extent and severity of the radical operation for mammary cancer calls for a positive diagnosis in every case. Since women are now coming earlier for diagnosis of mammary disease, and often before the characteristic clinical symptoms of established cancer have developed, the diagnosis of these conditions has become more difficult and biopsies are more frequently required.

The practice of removing apparently benign nodules from the breast in a doctor's office and waiting two or three days for a report from a distant pathologist often leads to serious situations, and, in the opinion of some surgeons, may imperil the patient's chances for a cure even by a radical operation. The mechanical trauma from such a biopsy may well dislodge cancer cells and cut across and loosen cancerous lymphatics, while the delay of some days gives opportunity for the dislodged cells to reach the distant lymph nodes. The hyperemia of the inflammatory process may also stimulate tumor growth and facilitate the local growth and even the dislodgement of more active tumor cells. There have been some observations which indicate that these undesirable events actually occur, and it is reasonable to assume that they do occur. Therefore the conservative surgeon will not remove a tumor nodule from the breast except in a surgical operating room where he is prepared to have an immediate diagnosis made and the proper operation performed at the same time.

There is a difference of opinion regarding the best method of performing the operation for a biopsy of the breast. Some surgeons prefer to cut directly into the tumor, make the diagnosis on the gross appearance which is usually specific, or cut out a piece of the tumor for frozen section. If the tumor proves to be cancer, the wound is closed over a sponge soaked in 10% formalin. They then discard the instruments and gloves used in the exploration, prepare the skin anew, and proceed with the operation indicated. This is a very direct and expeditious method. It avoids much trauma inevitable in a local excision which requires cutting on all sides of the tumor nodule. In the case of bulky tumors, it may be the best method.

In the case of small tumors, I think it is safer to remove the whole tumor, together with a wide area of normal breast tissue, using extreme care not to squeeze or roughly handle the cancerous mass. This procedure avoids cut-

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ting into cancerous tissue, and if it is done with extreme care not to squeeze the tumor, cancer cells should not be dislodged.

An experienced surgeon or pathologist should be able to recognize the great majority of malignant tumors of the breast by gross examination of the cut surface of the tumor. Unless he can do this it is obvious that the tissue chosen for microscopic section may not contain the malignant tumor. Therefore great importance attaches to the gross diagnosis, which should be relied upon wherever possible. The extent of the disease also can be told only by gross examination. The cicatricial character, resistance, opacity or translucency, and the chalky streaks of carcinoma are generally specific. Frozen section is therefore often unnecessary but should be made in all cases which are in any respect doubtful to the particular surgeon or pathologist concerned. This diagnosis should be made at the operation and the appropriate procedure carried out immediately.

There are some lesions in the breast in which it is difficult for any surgeon or pathologist to state positively whether the condition is malignant or benign. Hence the surgeon must not assume that by obtaining a microscopic diagnosis he has secured positive information. In such cases the clinical data, age of patient, extent and duration of the disease, condition of lymph nodes, and especially the gross characters of the lesion should be given much importance in the decision. Under these circumstances some surgeons would err on the side of caution and perform the radical operation. I believe it is unfair to the patient to perform a radical mestectomy unless the diagnosis of carcinoma is positive. There are many precancerous and suspicious lesions in the breast which are clinically benign, while a true carcinoma is nearly always obvious to a pathologist of adequate experience. When a substantial doubt exists about the nature of a microscopic section of a breast tumor, it is generally not cancer.

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